REMARKS

Claims 11, 12, 14-18 and 20 are pending in the above-identified patent application. Claims 11, 12, and 14-17 have been amended. Amendments to Claims 14-17 are introduced to correct clerical errors, and are merely formal in nature. No new matter has been added by these amendments.

Status of Claims

Applicants respectfully acknowledge that Claim 18 was absent from the list of claims included in the February 10, 2003, Response to First Office Action. Claim 18 (withdrawn) is included in the list of claims submitted herewith.

35 U.S.C. §112, first paragraph

Claims 12 and 14-17 are rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. The Office Action asserts, "the specification, while being enabling for 'active' fragments comprising Kunitz-3 domain, does not reasonably provide enablement for any 'active fragments of Kunitz-3 domain.'" Applicants respectfully traverse the rejection.

Applicants assert that the specification is enabling for any active fragment of the Kunitz-3 domain. The specification states on page 5, lines 1-6, that "[t]he composition provided herein contain[s] a protein known as "tissue factor pathway inhibitor" (TFPI), a TFPI homolog, or an active fragment thereof, wherein the fragment is defined by its ability to exhibit antiproliferative activity on human and other animal endothelial cells." The specification additionally states on page 7, lines 17-19, that "[a]ctive fragments of TFPI are

active portion thereof most probably plays an important role affecting the activity of TFPI or the binding of TFPI to its receptor on the surface of the endothelial cells" (emphasis added). On pages 11 and 12 (section *TFPI Fragments*) the specification teaches how to produce TFPI fragments and test them for antiproliferative activity. Furthermore, the techniques and methods for producing and testing such fragments are known to those skilled in the art. Therefore, the teachings in the specification regarding antiproliferative TFPI fragments containing the Kunitz-3 domain, and the techniques and methods for producing and testing TFPI fragments, are sufficient to enable one skilled in the art to make and use any active fragment of the Kunitz-3 domain. In view of the foregoing, Applicants respectfully request withdrawal of this rejection.

Claim Rejections under 35 U.S.C. §102(a)

Claims 11-17 and 19 are rejected under 35 U.S.C. §102(a) as anticipated by Steinhubl *et al.* (J. Amer. College of Cardiology 29 (2), 243A, 1997) or Khouri *et al.* (Surgical Forum 46, 389-391, 1995). The Office Action states "[I]f the prior art teaches the identical chemical structure and composition, the properties applicant discloses and/or claims are necessarily present." Applicants traverse this rejection.

Both Steinhubl *et al.* and Khouri *et al.* teach the inhibition of neointimal proliferation by a whole TFPI molecule. In contrast, Claim 11, as currently amended, recites a Kunitz-3 domain fragment of a tissue factor pathway inhibitor. The TFPI molecule is a protein molecule having a molecular weight of between approximately 32 kilodaltons and 45 kilodaltons, and having a structure of approximately 276 amino acids (see page 5, lines 6-9, of the specification). In contrast, the Kunitz-3 domain is a fragment of approximately 50 amino acids (see SEQ ID NO:1). Therefore, the molecules disclosed in Steinhubl *et al.* and

nor Khouri *et al.* teach the use of fragments of TFPI, nor do they suggest that fragments of TFPI could be useful. Therefore, neither Steinhubl *et al.*, nor Khouri *et al.* teach all aspects of the composition of the present invention as currently claimed.

Applicants respectfully assert the compositions of the present invention as claimed in currently amended Claim 11, and in Claims 12-17, and 19, dependent from Claim 11 and containing all the limitations thereof, are not *prima facie* anticipated by or obvious over Steinhubl *et al.* or Khouri *et al.*

In view of the amendment to Claim 11 and the foregoing remarks, applicants respectfully submit that the rejection has been overcome and request its withdrawal.

35 U.S.C. §103(a)

Claim 20 is rejected under 35 U.S.C. §103(a) as obvious over Steinhubl *et al.* or Khouri *et al.* As stated above, neither Steinhubl *et al.*, nor Khouri *et al.* teach the composition of the present invention as claimed in currently amended Claim 11 and claims dependent therefrom. Claim 20 is dependent on Claim 11 and contains all the limitations thereof. Steinhubl *et al.* or Khouri *et al.*, alone or in combination, do not teach all of the limitations of the Applicants' invention as claimed in Claim 20. Neither Steinhubl *et al.* nor Khouri *et al.* teach, suggest, or provide motivation to derive the compositions of the present invention as claimed in Claim 20. Applicants respectfully assert that Claim 20 as amended is therefore not obvious over Steinhubl *et al.* or Khouri *et al.*

In view of the amendment to Claim 11 and the foregoing remarks, Applicants respectfully submit that the rejection of Claim 20 has been overcome and request its

CONCLUSION

The foregoing is submitted as a full and complete response to the Final Office Action mailed April 22, 2003. Applicants respectfully submit that the claims are fully enabled, novel and non-obvious over the cited art. Applicants assert that the claims are now in condition for allowance and respectfully request that the application be passed to issuance. If the Examiner believes that any informalities remain in the case, which may be corrected by Examiner's amendment, or that there are any other issues which can be resolved by a telephone interview, a telephone call to the undersigned attorney at (404) 815-6500 is respectfully solicited.

Respectfully submitted,
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